Letter

Conclusions regarding the efficacy of treatments for neuroleptic malignant syndrome should be tempered given poor quality data, regardless of the analysis conducted

Darren M Roberts[1,2] and Jason A Roberts[3,4]

[1]South Asian Clinical Toxicology Research Collaboration, Medical School, Australian National University, PO Box 5141, Kingston, Australian Capital Territory, Australia, 2604
[2]Department of Clinical Pharmacology and Toxicology, The Canberra Hospital, PO Box 5141, Kingston, Australian Capital Territory, Australia, 2604
[3]Burns, Trauma and Critical Care Research Centre, University of Queensland, Level 3 Ned Hanlon Building, Royal Brisbane and Women's Hospital, Butterfield St, Herston QLD Australia 4029
[4]Departments of Intensive Care Medicine and Pharmacy, Level 3 Ned Hanlon Building, Royal Brisbane and Women's Hospital, Butterfield St, Herston QLD Australia 4029

Corresponding author: Darren Roberts, dmroberts@iprimus.com.au

Published: 2 May 2007
This article is online at http://ccforum.com/content/11/3/413

Critical Care 2007, **11:**413 (doi:10.1186/cc5786)

See related research by Reulbach *et al*., http://ccforum.com/content/11/1/R4

We read with interest the analysis by Reulbach and colleagues regarding the treatment of neuroleptic malignant syndrome (NMS) [1]. In this analysis, the effect of various treatments on clinical outcomes from 271 single case reports was reviewed. It was concluded that dantrolene does not seem to be the evidence-based treatment of choice for NMS.

We have concerns about the methodology employed by the authors, in particular the type of studies included in this analysis. Guidelines for grading the quality of evidence and strength of recommendations for the efficacy of an intervention were recently published, in which the analysis of single case reports is not a recognized approach for evaluating a treatment's efficacy [2]. Furthermore, case series were specifically excluded by Reulbach and colleagues, even though these studies can demonstrate the spectrum of severity and response to treatment, which is more informative. Other shortcomings in the methodology were also observed, and although some were acknowledged by the authors, clinical recommendations were still made.

We acknowledge the difficulties in the treatment of NMS given that the available data are restricted to case reports and small case series and agree that large prospective studies are probably impracticable. However, only limited conclusions can be drawn from any analyses of these data even if 'meta-analysis techniques' are used. This paper is valuable for hypothesis generation and we hope that it will stimulate further discussion. However, recommendations that influence the use of selected agents in the clinical management of NMS are not appropriate on the basis of the present study.

Authors' response

Udo Reulbach, Carmen Dütsch, Teresa Biermann, Wolfgang Sperling, Johannes Kornhuber and Stefan Bleich

We are inclined to agree with Roberts and Roberts concerning the difficulty in the assessment of the treatment of NMS.

We discussed the inclusion of case series. On the one hand, information was lost by the exclusion of those studies. On the other hand, this was the sole way to avoid biases resulting from multiple recorded case reports. In our opinion, this disadvantage outweighs the advantage. Unfortunately, publication bias is an inescapable feature of reviews or meta-analysis.

As a matter of course, the evidence level of such analyses is dependent on the quality of the studies analysed. As the data are restricted to case reports, it is not feasible to draw definite recommendations.

NMS = neuroleptic malignant syndrome.

Regarding the main objection by Roberts and Roberts, we did not recommend specific selected agents. In the past, dantrolene has been considered the treatment of choice. This recommendation, which was based on case reports or case series, could not be confirmed by our analysis, at least in part.

Competing interests

The authors declare that they have no competing interests.

References

1. Reulbach U, Duetsch C, Biermann T, Sperling W, Thuerauf N, Kornhuber J, Bleich S: **Managing an effective treatment for neuroleptic malignant syndrome.** *Crit Care* 2007, **11:**R4.
2. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, *et al.*: **Grading quality of evidence and strength of recommendations.** *BMJ* 2004, **328:**1490-1494.